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EXCRETION STUDIES, TOTAL BODY RADIATION, AND RADIATION TO THE BLOOD IN PATIENTS TREATED WITH RADIOACTIVE PHOSPHORUS (P^{32}) FOR POLYCYTHEMIA RUBRA VERA

A THESIS

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OF MASTER OF SCIENCE

DEPARTMENT OF RADIOLOGY

by

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FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "Excretion studies, total body radiation, and radiation to the blood in patients treated with radioactive phosphorus (P^{32}) for polycythemia rubra vera" submitted by Dorothy L. Weijer-Tolmie, B.Sc., in partial fulfilment of the requirements for the degree of Master of Science.

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ABSTRACT

Excretion studies were carried out on a series of 14 patients. In 11 cases P^{32} was administered intravenously and in 3 cases orally, under strict fasting conditions. In all cases the radio-phosphorus was carrier free and no additional carrier was administered. Under these conditions the fecal excretion was found to be low. The average urinary excretion of P^{32} for the entire series was 14.7% in 3 days, and the average fecal excretion 1.4% for the same period. From consideration of other published studies it would appear that carrier will tend to increase the urinary excretion after intravenous dosage and food and carrier will both increase fecal excretion after oral administration.

By observing strict fasting conditions and using carrier free P^{32} it should be possible to administer the same therapeutic dose of P^{32} either intravenously or orally to obtain the same clinical results. That is to say, under the above conditions an increase of 33% as often recommended in the oral dose is not necessary.

Radiation to the blood calculated in 16 cases was found to lie between 1.93 rad/mc. and 8.78 rad/mc. administered.

Total body radiation varied from 5.33 - 6.36 rad/mc. as a possible lower limit and 8.24 - 9.89 rad/mc. administered as the range of the possible upper limits.

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INTRODUCTION

A search of the literature (1-35) revealed only a small number of patients treated for polycythemia rubra vera with radioactive phosphorus in whom the excretion of P^{32} in both urine and feces had been followed (7). Some early references also dealt with tracer studies in normal persons (4, 10). It is unlikely that the P^{32} in these reports (prior to 1945) was manufactured carrier free and in most cases it was stated that administration was accompanied by additional carrier. These excretion figures are quoted without exception by all subsequent authors. In none of the oral cases and only one of the intravenous cases is there reference to the patient being kept in a fasting state before and after administration of dose. It was felt that both the amount of carrier added to the P^{32} (in the case of the oral and intravenous route) as well as the fasting or non-fasting condition of the patient (in the case of the oral route) would affect the excretion rates.

We considered that further knowledge of excretion rates in patients treated with the currently used carrier free P^{32}, both orally and intravenously, would be of significance in view of the clinical schedules of dosages for polycythemia rubra vera given by accepted authorities (1, 2, 5, 8, 26, 27, 33, 34) all of whom state that when used orally, the dose of P^{32} administered should be increased by a factor of $\frac{4}{3}$ to compensate for the 25% - 33% of the dose not absorbed by the gastrointestinal tract. Some of the authorities (1, 33, 34) even specify the above increase under strict fasting conditions before and after therapy.

It was thought worthwhile to follow a series of patients treated with carrier free P^{32} for as long as feasible and employ liquid counting methods available only since 1948 (i.e., subsequent to the original work on this topic).

Treatment of polycythemia rubra vera with P^{32} is successful between a relatively wide range of clinical dose levels. These dose levels have been arrived at by experience over the years and are not yet on a scientific basis. Very little is known of the underlying action of P^{32} on bone marrow. However, with the present day stress on genetic hazard to man from radiation and the possibility of leukaemogenic effects of P^{32} it becomes increasingly important to assess the individual total body radiation in patients treated. It is also important to keep the dosage low and to repeat it as infrequently as possible. The general theory for total body radiation has been worked out by Hine and Brownell (11); Quimby (26) refined this to some extent but used the conclusions and average excretion figures of the small series of Erf and Lawrence (7, 19). We have developed the basic dosimetry further in this paper. We then applied this to each case studied using the individual radioactive phosphorus excretion rate and body mass.

The activity of P^{32} in the blood was also followed and the radiation levels to the blood calculated to attempt a link between these levels and the results of therapy.

MATERIALS AND METHODS

From September 8, 1959, to June 10, 1961, twenty-four patients were admitted to the University Hospital for therapy with radioactive phosphorus; twenty-two of whom were diagnosed as having polycythemia rubra vera, one (T.H. No. 9) diagnosed as malignant pheochromocytoma, and one (H.S. No. 14) diagnosed as acute dermatitis. The radioactive phosphorus was administered intravenously in seventeen cases and orally in seven cases. The mode of the individual administration is indicated in Tables 5 and 9. The intravenous doses ranged from 3.5 - 4.5 millicuries and the oral doses ranged from 0.5 - 6.0 mc. The specific activity of the P^{32} varied from .72 - 2.85 mc/ml. at time of dose. It was contained in a sterile physiological salt solution in the form of sodium acid radio-phosphate ($Na_2HP^{32}O_4$) to which benzyl alcohol had been added as a preservative. The isotope was carrier free. It was obtained from Charles E. Frosst, Ltd., under Atomic Energy Commission license (see also Appendix I). In all cases the P^{32} was administered to the patient by the Radiotherapist.

Excretion Studies

All patients were confined to their room or ward for a minimum period of 5 days following treatment and they were instructed to collect their total urine output in the bottles provided. Large Kellner sealer jars were provided for each 8 hr. period covering the first 2 days and after this initial period a bottle (and a spare), was provided for each successive 24 hr. period.

Patients were held responsible for their own urine collection but the nursing staff assisted with the collection of stool which was transferred from bedpans to cardboard containers lined with plastic bags. None of the specimens were allowed to accumulate on the nursing stations but were removed at the end of the allotted time period, or in the case of the stool, were removed each morning or on receiving a call from the station. Powdered carrier (2 - 5 g.) in the form of trisodium phosphate was added to all urine bottles to prevent adsorption of P^{32} on the glass walls. Stool specimens were kept frozen until the time of preparation for counting. Patients with polycythemia were checked as carefully as possible for memory lapses which would lead to loss of specimens by their inadvertent use of hospital toilets.

Urine and stool collection was continued for at least 5 days and where possible for longer. Although 23 patients were studied, only 14 cases are presented in Tables 4 and 5. The other excretion studies were discarded because in some cases it was obvious and in other cases highly probable that all the urine specimens or stool had not been kept. Where any reasonable doubt existed the study was excluded from the final series.

Preparation of Excretion Specimens

The total volume of urine passed in each time period was measured. One, two or five ml. were withdrawn and diluted to 100 ml. with water after careful shaking of the specimen. The P^{32} content of the urine was greatest in the first 24 hrs., and it was usually

necessary to dilute 1 ml. of urine to 100 ml. in order to avoid counting losses due to coincidence of incident counts in the geiger tube. For specimens originating 24 hrs. or more after therapy, a dilution of 1:50 was sufficient because of the decreased content of P^{32} in the urine. Sodium triphosphate (1 g./100 ml.) was added to all diluents to prevent adsorption of P^{32} on the walls. These were well stoppered to prevent evaporation and stored until time of counting. The stool specimens were defrosted and homogenized individually in a large sized Waring blender with sufficient warm water to bring the total volume to 4,000 ml. Ten ml. was withdrawn by dipping a small container into the blender immediately after it was turned off and pouring this homogenate quickly into the counting tube.

Blood Studies

All patients had complete haematological studies including blood volume calculation before treatment but these results will not be fully reported at this time. In order to estimate the amount of radioactive phosphorus circulating in the patients' blood stream (and hence calculate the radiation to the blood from a therapeutic dose of P^{32}), heparinized venous blood samples were obtained so that the μc./ml. circulating P^{32} could be measured. 4 ml. whole blood was removed at intervals starting 10 minutes after treatment and continuing beyond the end of the patients' stay in hospital. The number of blood samples removed depended very much on the ease with which they could be obtained from the individual patient. In general about eight specimens were obtained in the first 8 hours

and three per day for the next 4 days. Whenever possible, blood was also sent to us by mail over the next 3 weeks (two samples each week) by the patients' local physician. This was arranged successfully in all but three cases.

Preparation of the Blood Specimens

The heparinized blood specimens were carefully shaken and 1, 2 or 5 ml. withdrawn. This was diluted to 100 ml. with 1 g. sodium triphosphate added to prevent adsorption. Care was taken to drain and wash the pipette carefully during the diluting process because of the high viscosity of polycythemic blood. The dilutions were well stoppered and stored until time of counting.

All specimens were disposed of in accordance with the recommendations for waste disposal of P^{32} (23).

Preparation of Standards

One tenth of a ml. of radioactive phosphorus was removed from the shipment by means of a sterile microsyringe and added to 1,000 ml. of dilute trisodium phosphate (concentration 5 g/1,000 ml.). The initial 0.1 ml. represented 200 - 300 μc P^{32}. One ml. of this solution was withdrawn by means of a 1 ml. pipette and again diluted in 100 ml. solution of trisodium phosphate (concentration as before). The second dilution then contained between 0.02 and 0.03 microcuries P^{32}/10 ml. depending on the concentration in mc/ml. of the original shipment. This gave a count of the order of 4,000 cts/min/10 ml. of standard with the equipment described in the following section.

Urine and blood dilutions were counted against this standard, whereas a separate standard was prepared for the stool specimens. This latter was made up by adding a small amount of the standard used for counting urine and blood to a homogenate of non-radioactive stool. This was done in order to adjust for the loss of counts due to absorption of the Beta particles by the stool particles (see counting methods).

Equipment

A liquid G-M tube type M-6, capacity 10 ml., was used for sample counting in conjunction with a lead well and an Atomic Multi-scaler. This sample container consisted of a thin walled geiger tube made of glass drawn to a thickness just sufficient to withstand atmospheric pressure when the counter is evacuated or has a low pressure gas filling. The wall thickness is about 30 mg/cm.^{2} (.004 in. glass) and surrounded by an annulus which will accommodate a volume of 10 ml. For the reasonably high β energy of P^{32} this counter can be used to measure the activity of homogeneous fluid samples in the annulus of concentrations approximating .025 μc/10 ml. The counting efficiency is 5 - 10% for P^{32} with a background from 10 - 15 cts/min. As long as the annular space is filled with liquid above the level of the thin-walled section of the tube, the observed counting rate is substantially independent of the volume of the liquid employed and is directly proportional to the radioactive concentration. It is necessary to employ a standard of the same density and chemical composition as the sample.

FIGURE I

DIAGRAM OF LEAD CASTLE AND M-6 GEIGER TUBE

A. LEAD CASTLE

B. WELL FOR GEIGER TUBE

C. LIGHT PROOF LID

D. MERCURY IN PYREX TUBE

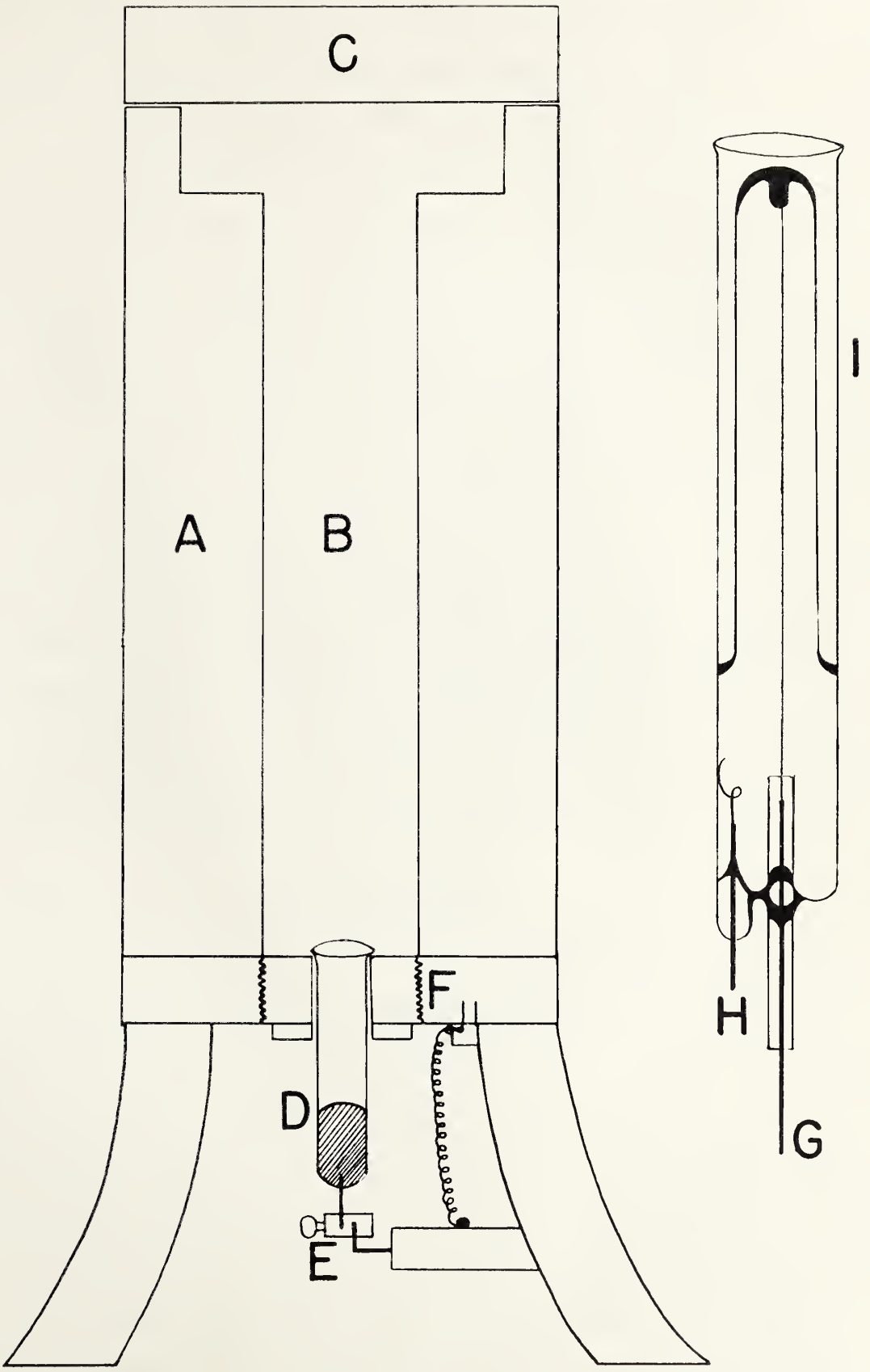
E. HIGH VOLTAGE TERMINAL

F. CONNECTION TO GROUND

G. ANODE

H. CATHODE

I. ANNULUS TO HOLD 10 ML.


C
A
B
D
E
F
H
G
I

A lead castle (see Figure 1) was designed to hold the M-6 tube. This had a cylindrical cross-section of 1" lead and central core with a light-proof lead lid. The M-6 tube was inserted into the central core of the lead castle in such a way that its terminals made contact with the terminals in the base of the castle. (That is to say, the central anode of the tube rested in a pyrex glass container filled with mercury to which high voltage was applied by means of a tungsten filament running through the glass container. The outer cathode wall of the β-counter was earthed by means of contact with a brass core.) These two terminals were in turn connected by a length of screened coaxial cable to the Geiger input of an Atomic Multiscaler which convert the pulses into counts per minute. The scale was set at a 1060v, selector 50, attenuator 4, throughout. The M-6 tube could be removed from the castle for filling, emptying and cleaning without switching off the H-T* supply and contact was automatically remade when the tube was reinserted.

Methods of Counting

After a preliminary check of the counting apparatus, with the voltage set at 100 volts above the threshold, the water blank background of the geiger tube was obtained (i.e., the tube was filled with tap water). This background over several hours of initial counting was found to be less than 1 count/sec. The specimens were then counted against the prepared standard for 5 min. each, to insure good statistics (standard error less than 5%). The counts were recorded as counts/5 min. 10 ml. Care was taken to thoroughly

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* High tension.

shake all specimens and standards before pouring them into the annular geiger tube. The stool homogenate was decanted from the Waring Blender, as soon as the blender was turned off, before any particles could settle.

The standard was counted before the first specimen, and at the end of each sequence of specimens if the time involved was greater than 3 hours. The geiger tube itself was thoroughly cleansed between every count to avoid any contamination from the previous specimen. (This usually involved one careful rinse with water and an acid solution, and a one minute check on the counting rate.) In general, the dilution of the specimens previously described insured a reasonable counting rate, but where the rate was more than 140 counts/sec. (i.e., 1% loss of counts), corrections were made to allow for these losses which were due to coincidence of incoming counts in the geiger tube. This correction was made from a coincidence loss curve for the particular type of G.M.* tube being used.

Total Body Radiation from Radioactive Phosphorus (T.B.R.)

The phrase "total body radiation" properly refers to a radiation dose homogeneous throughout the body. Since it is highly unlikely that the P^{32} is distributed uniformly (6, 8, 12, 13, 19, 22, 24), the body dose is not homogeneous and hence the phrase is not strictly applicable. Nevertheless, one may determine the total dose received by the body per unit mass and the result, which is the average value over the body, is what is meant by total body radiation in this paper.

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* Geiger-Muller.

We make the following simplifying assumptions:

1. The P^{32} not excreted or decayed is uniformly distributed throughout the body.
2. The body is homogeneous and of density unity.
3. The beta radiation from the body content of P^{32} is entirely absorbed within the body.
4. A smooth curve drawn through points obtained from excreted activity at times of collection, leads to a measure of activity in the body as a function of time.

Let M = body mass (kg)

I = activity of body content (mc)

E = average beta-particle energy (0.7 mev for P^{32})

D_t = body dose to time t (rad)

Rate of energy absorption per unit mass

$$= 3.7 \times 10^{7} \times 1.6 \times 10^{-6} \times \frac{3600}{100} \times \frac{IE}{1000\ M} \text{ rad/hr.}$$

$$= 2.1\ \frac{IE}{M} \text{ rad/hr.}$$

Thus $D_t = \frac{2.1\ E}{M} \int_0^t I\,dt$ rad (11, p. 824)

$$= \frac{1.47}{M} \int_0^t I\,dt \text{ rad} \quad (1)$$

FIGURE 2

BODY CONTENT OF P^{32} WITH RESPECT TO TIME, CORRECTED FOR EXCRETION AND DECAY (MR. D.S. No. 10)

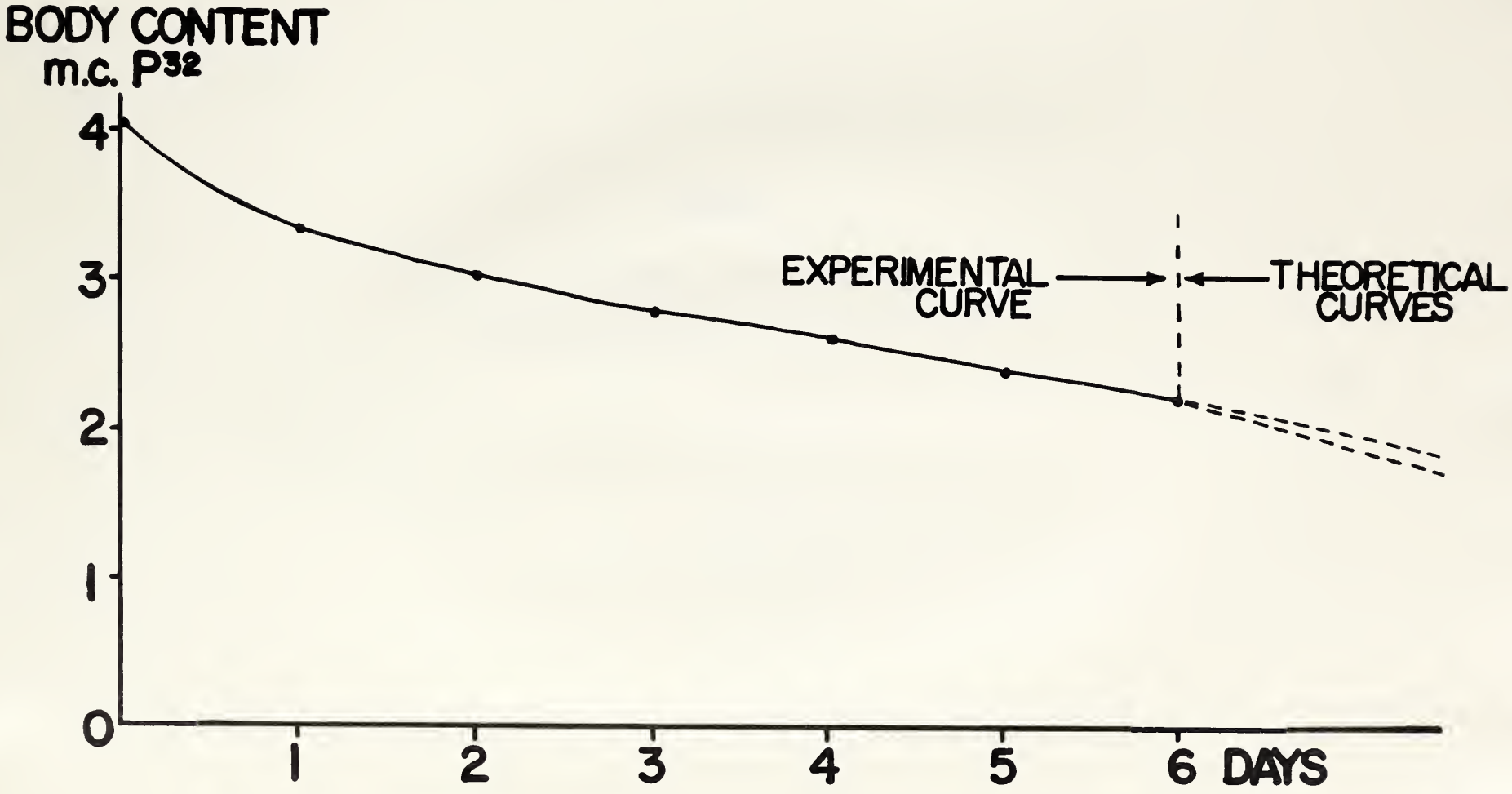
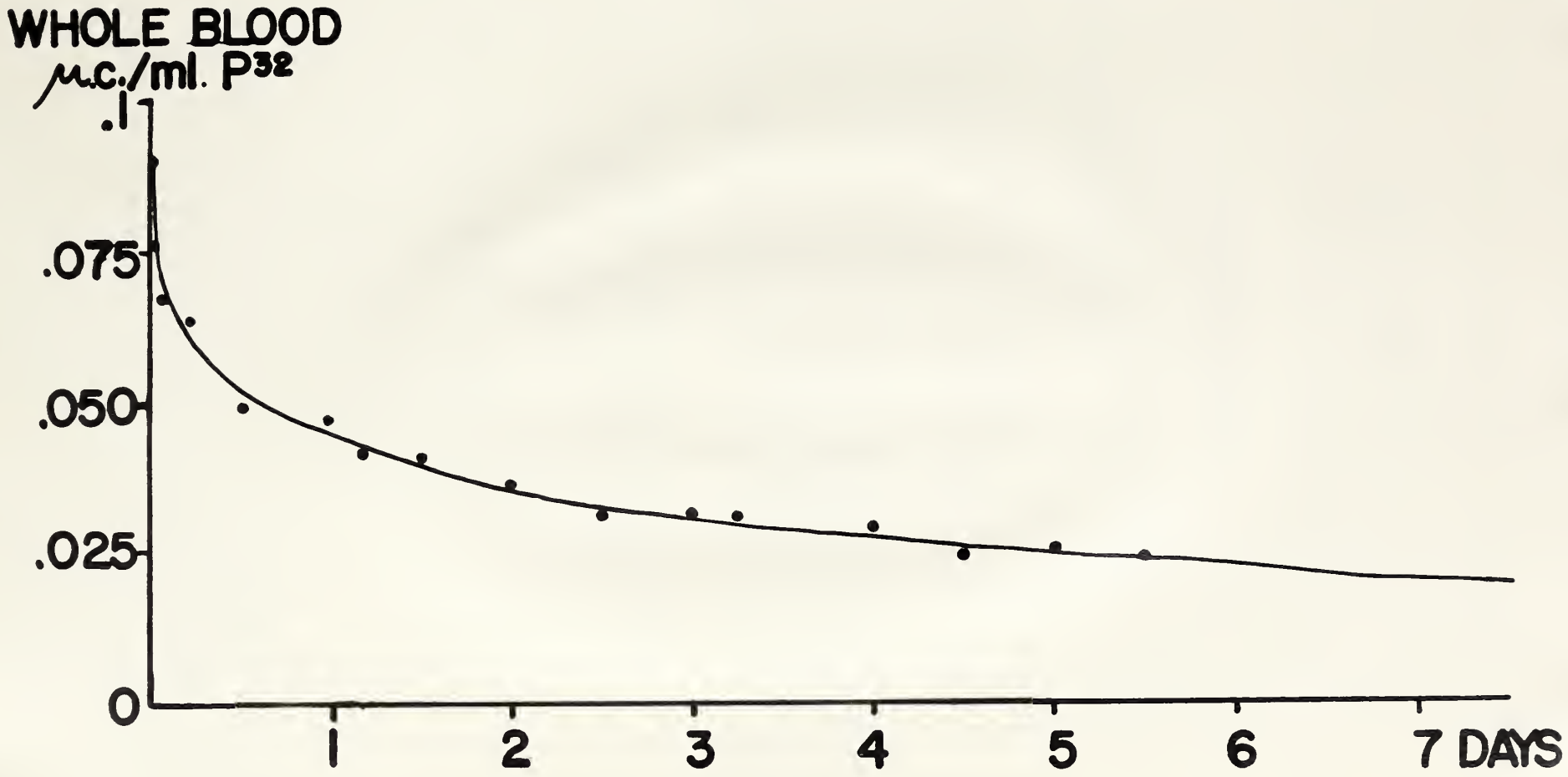

BODY CONTENT
m.c. P32
4
3
2
1
0
EXPERIMENTAL CURVE
THEORETICAL CURVES
1
2
3
4
5
6 DAYS

FIGURE 3

AMOUNT OF P^{32} IN WHOLE BLOOD WITH RESPECT TO TIME,

CORRECTED FOR DECAY (MR. D.S. No. 10)


WHOLE BLOOD
μc./ml. P32
.1
.075
.050
.025
0
1
2
3
4
5
6
7 DAYS

In order to evaluate the integral it was necessary to draw a curve showing the value of I as a function of time (hours) taking account of decay and both urinary and fecal excretion (Figure 2). The value of the integral is then the area under the curve to time t.

Radiation to the Blood

In calculating the radiation to the blood we make the following simplifying assumptions:

1. The blood is homogeneous and of density unity.
2. The beta radiation from the P^{32} blood content is entirely absorbed within the blood.
3. A smooth curve drawn through points obtained from whole blood content, at various times after administration of the dose, leads to a measure of activity in blood as a function of time.

If C is the concentration of P^{32} in whole blood ($\mu C/g.$ or $\mu C/ml.$) then, as in the previous section,

Dose rate = 2.1 E C rad/hr.

$$D_t = 2.1\ E\ C \int_0^t C\ dt \quad (2)$$

$$= 1.47 \int_0^t C\ dt$$

In order to evaluate the integral it is necessary to plot values of C as a function of time and to find the appropriate area under the curve (Figure 3).

RESULTS

Total Body Radiation

In order to calculate the total body radiation, the daily excretion of P^{32} for each person studied had first to be found. The method is illustrated for one particular patient (Mr. D.S.) in Tables I and 2. These values were then used to plot the total body content with time (Figure 2, Table 3). Table 4 gives the daily excretion for the complete series of 14 patients. Their respective total body contents are plotted in Figure 4. The total body radiation is in each case directly proportional to the area enclosed by these individual curves. For the first 6 days the integral in equation (1) was determined from the experimental curves (first part of Table 5) but from 6 days onwards the area had to be estimated.

Usually a polycythemia patient is hospitalized for only 6 days. Neither the P^{32} body content nor excretion has reached zero during this time. A survey of the literature revealed no published data on excretion beyond 6 days, although Lawrence (14) postulated in his summary on dosimetry following intravenous P^{32}, that from the third day, bone and soft tissue lose P^{32} through excretion and decay at the rate of 6.1% per day corresponding to an effective half life of 11 days.

In order to try to resolve this problem to some degree we followed a series of 4 orthopedic patients given tracer doses of P^{32}

TABLE I

EXPERIMENTAL RECORD AND CALCULATIONS USED FOR THE DETERMINATION OF EXCRETION OF P^{32} IN THE URINE OVER THE FIRST SIX DAYS AFTER THERAPY

(Mr. D.S., No. 10)

* All counts shown are averages of three, two minute counts

NAME: Mr. D.S.
DIAGNOSIS: Polycythemia rubra vera
ISOTOPE USED: P^{32}
DOSE GIVEN: 4.00 mc., 6 November 1959 at 0930
CORRECT AS OF: Time of Dose
DATE OF COUNTING: 12 November 1959
TIME COUNTING STARTED: 0700 hrs.
TYPE OF SPECIMEN: Dilutions of urine

TUBE NO. P. 1287
SELECTOR 50
ATTENUATOR 4
VOLTAGE 1060

	Volume of total specimen (ml)	Dilution made	Count/* 2 min. 10 ml.	Back-ground	Corrected counts	µc/10 ml. of dilution	µc/10 ml. urine	Total µc in specimen	Total excretion of urine in µc/day	% of initial dose excreted each day (40 µc = 1%)
Standard Value = 0.0465 µc/10 ml.										
As of - time of dose			13,743	112	13,631					
Time of Specimen Collection after Therapy										
8 hours	780	1:50	20,174	110	20,064	0.0684	3.42	266.8	461.3	11.5
16 hours	1,040	1:50	11,071	107	10,964	0.0374	1.87	194.5		
32 hours	620	1:50	8,592	87	8,505	0.0290	1.45	89.9		
40 hours	740	1:50	5,522	60	5,462	0.0186	0.93	68.8	168.6	4.2
2 days	220	1:50	2,716	71	2,645	0.00900	0.45	9.9		
3 days	1,480	1:50	3,512	69	3,443	0.0117	0.59	88.8	88.8	2.2
4 days	1,700	1:50	3,275	50	3,225	0.0110	0.55	93.5	93.5	2.3
5 days	1,600	1:50	2,477	73	2,404	0.00820	0.41	65.6	65.6	1.6
6 days	1,500	1:50	1,464	58	1,406	0.00450	0.24	36.0	72.5	1.8
6 days (extra bottle)	960	1:50	2,250	61	2,189	0.00750	0.38	36.5		

TABLE 2

EXPERIMENTAL RECORD AND CALCULATIONS USED FOR THE DETERMINATION OF EXCRETION OF P^{32} IN THE STOOL OVER THE FIRST SIX DAYS AFTER THERAPY

(Mr. D.S., No. 10)

* All counts shown are averages of three, two minute counts

NAME: Mr. D.S.
DIAGNOSIS: Polycythemia rubra vera
ISOTOPE USED: P^{32}
DOSE GIVEN: 4.00 mc., I.V., 6 November 1959 at 0930
CORRECT AS OF: Time of dose
DATE OF COUNTING: 13 November 1959
TIME COUNTING STARTED: 1300 hrs.
TYPE OF SPECIMEN: Homogenate of stool

	Volume of stool homogenate	Cts/2 min.* 10 ml.	Background /2 min.	Corrected counts	µc/10 ml. dilution	Total µc content	% of initial dose excreted per day 40 µc = 1%
Standard for Stool = 0.0465 µc/10 ml.							
As of - time of dose		13,404	104	13,300			
Sampling Time							
1 Day	4,000	12,474	94	12,380	0.0433	17.3	0.46
2 Days	4,000	10,611	61	10,550	0.0370	14.8	0.37
3 Days	4,000	8,376	87	8,289	0.0290	11.6	0.29
4 Days	4,000	792	102	690	0.00241	1.0	-
6 Days	4,000	11,470	112	11,358	0.0397	15.9	0.40
					TOTAL	60.6	1.52

TABLE 3

CALCULATION OF TOTAL BODY CONTENT OF P^{32}

FOR THE FIRST SIX DAYS AFTER THERAPY

(Mr. D.S., No. 10)

	Initial body content	Amount excreted daily (μc) (stool + urine)	Time after dose	Decay factor	Actual value excreted (μc)	Value of amount in body before excretion (mc)	Amount left in body after excretion (mc)
Patient: Mr. D.S.	4.024	478.6	1 day	0.9527	456.0	3.834	3.378
		183.4	2 days	0.9076	166.4	3.218	3.052
		100.4	3 days	0.8646	86.8	2.908	2.821
		94.5	4 days	0.8237	77.8	2.689	2.612
		65.6	5 days	0.7847	51.5	2.488	2.437
		88.4	6 days	0.7476	66.1	2.322	2.256

TABLE 4

DAILY EXCRETION OF P^{32} IN 14 CASES

(UNIVERSITY OF ALBERTA HOSPITAL)

* Non-polycythemic cases

** Oral Therapy

Case No.	Patient	Sex	Days Studied	Daily Excretion as % of Initial Dose								Total to End of 3 Days	Total to End of 5 Days
			Day	1	2	3	4	5	6	7	8		
1	H.C.**	F	6	Urine 4.0	1.5	0.9	0.5	0.6	1.8			6.4	7.5
				Stool -	1.4	0.2	0.4	0.7	0.6			1.6	2.7
				Total 4.0	2.9	1.1	0.9	1.3	2.4			8.0	10.2
2	L.M.	M	6	11.5	4.0	3.0	2.0	2.0	1.0			18.5	22.5
				0.8	0.5	0.5	0.5	0.3	-			1.8	2.6
				12.3	4.5	3.5	2.5	2.3	1.0			20.3	25.1
3	L.R.	M	6	5.4	2.7	1.5	2.0	1.8	1.5			9.6	13.4
				0.9	1.0	1.0	1.0	1.0	0.6			2.9	4.9
				6.3	3.7	2.5	3.0	2.8	2.1			12.5	18.3
4	W.M.	M	5	8.1	5.9	2.4	2.5	1.7				16.4	20.6
				0.3	0.3	0.3	0.3	0.3				0.9	1.5
				8.4	6.2	2.7	2.8	2.0				17.3	22.1
5	J.L.	M	5	9.6	2.9	3.6	2.6	2.2				16.1	20.9
				0.3	0.3	0.3	0.3	0.8				0.9	2.0
				9.9	3.2	3.9	2.9	3.0				17.0	22.9
6	T.M.	M	5	10.0	4.1	2.5	2.5	2.2				16.6	21.3
				-	-	1.3	-	1.3				1.3	2.6
				10.0	4.1	3.8	2.5	3.5				17.9	23.9
7	W.C.	M	5	7.6	4.0	3.0	2.0	1.0				14.6	17.6
				-	0.8	0.5	0.3	-				1.3	1.6
				7.6	4.8	3.5	2.3	1.0				15.9	19.2
8	T.K.	F	5	9.4	3.3	2.1	1.5	1.0				14.8	17.3
				-	0.5	0.7	0.7	0.7				1.2	2.6
				9.4	3.8	2.8	2.2	1.7				16.0	19.9
9	T.H.*	M	8	10.7	3.2	2.6	1.7	1.3	0.8	0.8	1.0	16.5	19.5
				-	0.3	0.7	1.0	0.8				1.0	2.8
				10.7	3.5	3.3	2.7	2.1				17.5	22.3
10	D.S.	M	6	11.5	4.2	2.2	2.3	1.6	1.8			17.9	21.8
				0.5	0.4	0.3	-	-	0.4			1.2	1.2
				12.0	4.6	2.5	2.3	1.6	2.2			19.1	23.0
11	C.H.	F	5	12.0	4.0	2.7	1.8	1.5				18.7	22.0
				-	0.5	1.0	0.5	-				1.5	2.0
				12.0	4.5	3.7	2.3	1.5				20.2	24.0
12	F.Mc.	F	6	12.0	2.6	2.4	2.1	1.8	1.3			17.0	20.9
				0.6	0.6	1.0	0.8	0.5	0.5			2.2	3.5
				12.6	3.2	3.4	2.9	2.3	1.8			19.2	24.4
13	E.L.**	F	8	10.0	2.6	2.0	1.5	1.4	1.0	0.9	0.8	14.6	17.5
				-	-	0.1	0.2	0.2	0.2	0.1	0.1	0.1	0.5
				10.0	2.6	2.1	1.7	1.6	1.2	1.0	0.9	14.7	18.0
14	H.S.*,**	M	22	6.5	0.9	0.9	0.7	0.6	0.5	0.7	0.9	8.3	9.6
				1.6	0.3	0.3	0.3	0.3	0.3	0.3	0.3	2.2	2.8
				8.1	1.2	1.2	1.0	0.9	0.8	1.0	1.2	10.5	12.4

FIGURE 4

BODY CONTENT WITH RESPECT TO TIME, CORRECTED FOR

EXCRETION AND DECAY

(14 CASES, UNIVERSITY OF ALBERTA HOSPITAL)

Nos. 1-14, inclusive, refer to the patients in Table 4

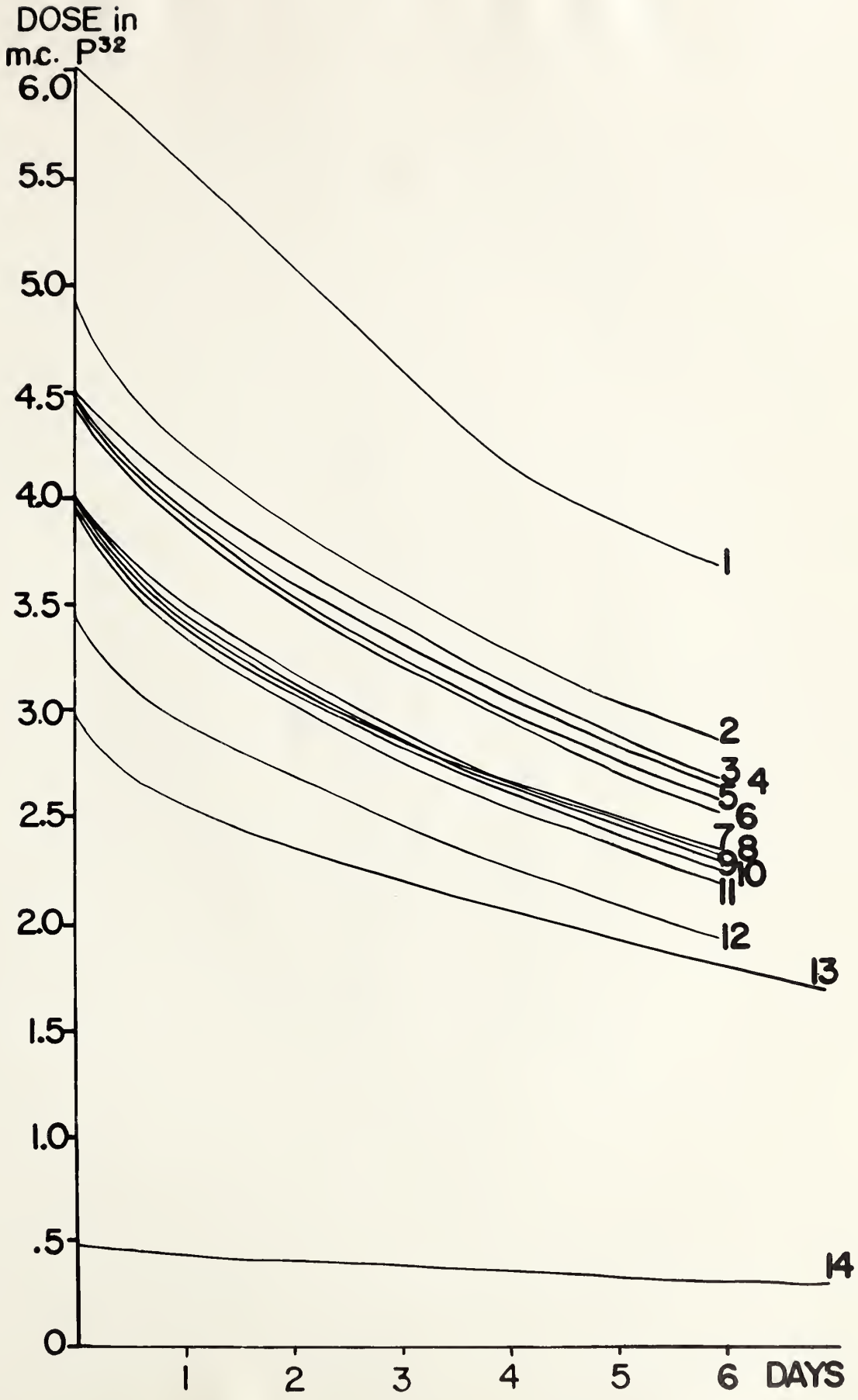

DOSE in
m.c. P32
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0
1
2
3
4
5
6
DAYS
1
2
3
4
5
6
7
8
9
10
11
12
13
14

TABLE 5

CALCULATION OF TOTAL BODY RADIATION FOR 14 CASES

(UNIVERSITY OF ALBERTA HOSPITAL)

* Non-polycythemic cases

** Oral therapy

*** Previous column $\times \frac{1.47}{M}$ (see equation (1), pages 11 and 23)

Case No.	Patient	Mass (Kg)	Dose (mc) Oral or I.V.	Area Under Curve to End of 6 Days (mc hrs.)	T.B.R. in First 6 Days (rad) A***	Assuming No Further Excretion After 6 Days			Assuming 1% Excretion After 6 Days			rad/mc. (A + B)	rad/mc. (A + C)
						Area Under Extrapolated Curve (6 Days - ∞) (mc hrs)	T.B.R. (6 Days - ∞) (rad) B***	T.B.R. A + B (rad)	Area Under Extrapolated Curve (6 Days - ∞) (mc hrs)	T.B.R. (rad) C***	T.B.R. A + C		
1	H.C.	61.00	6.07**	676.80	16.31	1813.75	43.71	60.02	1410.42	33.99	50.30	9.89	8.24
2	L.M.	70.00	5.00	528.36	11.10	1413.44	29.68	40.78	1099.13	23.08	34.18	8.15	6.84
3	L.R.	78.60	4.50	499.05	8.40	1324.48	24.56	32.96	1029.95	19.26	27.66	7.32	6.15
4	W.M.	71.80	4.50	487.15	9.97	1309.65	26.81	36.78	1018.42	20.85	30.82	8.17	6.85
5	J.L.	58.00	4.50	478.01	12.11	1275.06	32.32	44.43	991.52	25.13	37.24	9.87	8.28
6	T.M.	70.50	4.52	471.90	9.84	1245.41	25.97	35.81	968.46	20.19	30.03	7.92	6.64
7	W.C.	80.40	4.00	428.64	7.84	1161.39	21.23	29.07	903.13	16.15	24.35	7.27	6.09
8	T.K.	61.36	3.97	423.95	10.16	1146.57	27.47	37.63	891.60	21.36	31.52	9.48	7.94
9	T.H.*	56.40	4.00	423.36	11.03	1136.68	29.63	40.66	883.91	23.04	34.07	10.17	8.52
10	D.S.	88.60	4.00	416.76	6.91	1116.91	18.53	25.44	868.54	14.41	21.32	6.36	5.33
11	C.H.	57.30	4.00	408.70	10.67	1102.09	28.27	38.94	857.01	21.99	32.66	9.73	8.16
12	F.Mc.	77.30	3.50	362.94	6.90	948.88	18.04	24.94	745.56	14.18	21.08	7.13	6.02
13	E.L.	66.36	2.97**	321.42	7.12	884.64	19.60	26.72	687.91	15.24	22.36	9.00	7.53
14	H.S.*	55.50	0.48**	53.57	1.43	150.83	3.99	5.42	117.28	3.11	4.54	11.41	9.56

(the results will be published separately), and 2 patients with polycythemia rubra vera, for periods ranging from 8 - 24 days. From these results it appears that after 6 days a figure of 1% per day total excretion would not be exceeded but in most cases the excretion becomes much less than 1%. The minimum possible would, of course, be zero excretion. The effective half lives (from 6 days on) corresponding to these two extremes can be calculated as 11.1 and 14.3 days respectively*. We may then determine analytically the contribution to the integral, beyond the 6-day period, corresponding to each of these extremes. This gives at least a workable upper and lower range for the total body radiation between which it seems likely that the true individual values lie.

If I_6 is the body content on the sixth day (in mc, which can be read off the graph, Figure 4), we can write

$$\int_0^\infty I\,dt = I_6 \int_0^\infty e^{-\lambda t}\,dt$$
$$= \frac{I_6}{\lambda}$$

where λ is the relevant decay constant and the origin of time for this contribution is day 6.

---

* $$\frac{1}{\text{Effective half-life}} = \frac{1}{\text{Biological half-life}} + \frac{1}{\text{Radioactive half-life}}$$

$\therefore$ when we assume no further excretion after day 6, the effective half life = 14.3 days (viz., the radioactive half life of P^{32}). Similarly, when we assume a constant daily excretion of 1% of initial dose daily, $\frac{1}{\text{Biological half-life}} = \frac{1}{50}$ thence it can be shown that the effective half life = 11.1 days (i.e., fortuitously the same estimate as that of Lawrence (14)).

In the first case of zero excretion from day 6:

$$\lambda = \frac{0.693}{14.3 \times 24}$$

In the second case of 1% excretion from day 6:

$$\lambda = \frac{0.693}{11.1 \times 24}$$

Hence the area under the body content curve can be calculated by substituting $\frac{I_6}{\lambda}$ in equation (1) as follows:

$$D = \frac{1.47}{M} \frac{I_6}{\lambda} \text{ rad}$$

Results for Mr. D.S.

Dose = 4 mc.

I_6 = 2.26 mc.

M = 88.60 kg.

Area under experimental curve to end of 6 days = 416.76 mc. hrs.

$\therefore$ dose to end of day 6 = $\frac{1.47 \times 416.76}{88.60}$ rad

= 6.91 rad

(a) Assuming no further excretion

Dose from 6 days to total decay (∞) = $\frac{1.47}{88.60} \times \frac{2.26}{0.693} \times 14.3 \times 24$ rad

= $\frac{1.47}{88.60} \times 1116.91$ rad

= 18.53 rad

(b) Assuming 1% excretion from day 6

$$\text{Dose from day 6 to total decay } (\infty) = \frac{1.47}{88.60} \times \frac{2.26 \times 11.1 \times 24}{0.693}$$

$$= \frac{1.47}{88.60} \times 868.54 \text{ rad}$$

$$= 14.41 \text{ rad}$$

∴ the T.B.R. from time of dose to complete decay lies between 21.32 and 25.44 rad or 5.33 and 6.36 rad/mc. administered. This was repeated for the series of 14 patients and the results are given in Table 5.

Radiation to the Blood

The amount of P^{32} present in whole blood was calculated from individual specimens in 16 patients. The calculations are shown for Mr. D.S. in Tables 6 and 7. The blood content curve was plotted directly from these results (Figure 3). The radiation to the blood is directly related to the area (in μc hrs.) under this curve (equation (2)). In all cases the curve was extrapolated to zero by means of estimating the effective half life of the activity in the blood from the semi-log plot*.

In some cases the plasma level of P^{32} was followed (Table 8) and it was found that the P^{32} was rapidly removed in the first 24 hrs. (Figure 5).

---

* Figures 5 and 6 show in semi-log plot the variation with time of P^{32} in blood after oral and intravenous administration. In the latter case the plasma level was also followed.

Results from Mr. D.S.

Area under curve = 12.84 μc hrs/ml.

∴ total dose to blood = 1.47 × 12.84 rad

= 18.87 rad

i.e., 4.72 rad/mc. administered

The results for the series of 16 patients are shown in Table 9 together with some hematological data.

TABLE 6

EXPERIMENTAL RECORD AND CALCULATIONS USED TO DETERMINE THE AMOUNT OF P^{32} IN WHOLE BLOOD AFTER THERAPY

(Mr. D.S., No. 10)

* All counts shown are averages of three, two minute counts.

NAME: Mr. D.S.
DIAGNOSIS: Polycythemia rubra vera
ISOTOPE USED: P^{32}
DOSE GIVEN: 4.00 mc. I.V., 6 November 1959 at 0930
CORRECT AS OF: Time of dose
DATE OF COUNTING: 9 November 1959
TIME COUNTING STARTED: 1400 hrs.
TYPE OF SPECIMEN: Dilutions of whole blood

TUBE NO. P. 1287
SELECTOR 50
ATTENUATOR 4
VOLTAGE 1060

	Counts per 2 min.* /10 ml.	Background /2 min. /10 ml.	Corrected counts	µc/10 ml. of dilution (2:100)	µc/10 ml. whole blood	Decay factor	True µc content of blood /10 ml.
Standard Value = 0.0465 µc/10 ml.							
As of - time of dose	16,207	61	16,146				
Sampling Time							
10 minutes	6,297	54	6,243	0.01798	0.899	1.000	0.90
20 minutes	5,417	60	5,357	0.01543	0.772	1.000	0.77
30 minutes	4,651	51	4,600	0.01325	0.663	1.000	0.66
45 minutes	3,850	73	3,777	0.01088	0.544	1.000	0.54
1 hour	3,671	60	3,611	0.01040	0.520	1.000	0.52
3 hours	3,295	80	3,215	0.00926	0.463	0.994	0.46
8 hours	3,539	74	3,465	0.00998	0.499	0.982	0.49
12 hours	3,275	68	3,201	0.00922	0.461	0.976	0.45
24 hours	3,124	62	3,062	0.00882	0.441	0.953	0.42
28 hours	2,989	58	2,931	0.00844	0.422	0.947	0.40
32 hours	3,044	72	2,972	0.00856	0.428	0.935	0.40

TABLE 7

CONTINUATION OF EXPERIMENTAL RECORD AND CALCULATIONS USED TO DETERMINE THE AMOUNT OF P^{32} IN WHOLE BLOOD AFTER THERAPY

(Mr. D.S., No. 10)

* All counts shown are averages of three, two minute counts

NAME: Mr. D.S.
DIAGNOSIS: Polycythemia rubra vera
ISOTOPE USED: P^{32}
DOSE GIVEN: 4.00 mc. I.V., 6 November 1959 at 0930
CORRECT AS OF: Time of dose
DATE OF COUNTING: 12 November 1959
TIME COUNTING STARTED: 0900 hrs.
TYPE OF SPECIMEN: Dilutions of whole blood

	Counts per 2 min.* /10 ml.	Background /2 min. /10 ml.	Corrected counts	µc/10 ml. of dilution (2:100)	µc/10 ml. whole blood	Decay factor	True µc content of blood /10 ml.
Standard Value = 0.0465 µc/10 ml.							
As of - time of dose	13,736	100	13,636				
Sampling Time							
36 hours	2,516	82	2,434	0.00830	0.419	0.930	0.39
48 hours	2,536	79	2,457	0.00838	0.419	0.908	0.38
60 hours	2,243	61	2,182	0.00744	0.372	0.886	0.33
72 hours	2,247	77	2,170	0.00740	0.370	0.865	0.32
78 hours	2,183	54	2,129	0.00726	0.363	0.854	0.31
96 hours	2,127	62	2,065	0.00704	0.352	0.824	0.29
108 hours	1,893	69	1,824	0.00622	0.311	0.804	0.25
120 hours	1,945	80	1,865	0.00636	0.318	0.785	0.25
132 hours	1,831	72	1,759	0.00600	0.300	0.766	0.23
9 days + 12 hours	1,394	68	1,326	0.00452	0.226	0.620	0.14

TABLE 8

EXPERIMENTAL RECORD AND CALCULATIONS USED TO DETERMINE THE AMOUNTS OF P^{32} IN THE PLASMA DURING THE FIRST 24 HRS. AFTER THERAPY

(Mr. D.S., No. 10)

* All counts shown are averages of three, two minute counts

NAME: Mr. D.S.
DIAGNOSIS: Polycythemia rubra vera
ISOTOPE USED: P^{32} carrier free
DOSE GIVEN: 4 mc. I.V.
CORRECT AS OF: 09.30, 6 November 1959
TIME COUNTING STARTED: 0900 hrs., 10 November 1959
TYPE OF SPECIMEN: Dilutions of plasma

	Counts per 2 min.* /10 ml.	Background /2 min. /10 ml.	Corrected counts	µc/10 ml. of dilution (1:100 unless stated)	µc/10 ml. plasma	Decay factor	True µc content of plasma /10 ml.
Standard Value = 0.0465 µc/10 ml.							
As of - time of dose	15,601	71	15,530				
Sampling Time							
10 minutes	4,877	67	4,810	0.01440	1.44	1.000	1.44
20 minutes	3,669	62	3,607	0.01080	1.08	1.000	1.08
30 minutes	2,839	61	2,739	0.00820	0.82	1.000	0.82
45 minutes	2,162	58	2,104	0.00630	0.63	1.000	0.63
1 hour	1,054	52	1,002	0.00300	0.30	1.000	0.30
2 hours	6,417	71	6,346	0.01900 (1:10)	0.19	1.000	0.19
3 hours	5,770	59	5,711	0.01710 (1:10)	0.171	0.994	0.17
4 hours	5,103	60	5,043	0.01510 (1:10)	0.151	0.994	0.15
6 hours	3,427	54	3,373	0.01010 (1:10)	0.101	0.988	0.10
6 1/2 hours	2,492	57	2,435	0.00729 (1:10)	0.0729	0.988	0.07(2)
8 hours	1,827	54	1,733	0.00519 (1:10)	0.0519	0.982	0.05(1)
10 hours	903	51	852	0.00255 (1:10)	0.0255	0.982	0.02(5)
12 hours	21,357	101	21,256	0.63620 (1:1)	0.00636	0.976	0.006(2)
24 hours	5,020	110	4,910	0.14701 (1:1)	0.00147	0.953	0.001(4)

FIGURE 5

P^{32} CONTENT IN WHOLE BLOOD AND PLASMA RELATED TO TIME

AFTER INTRAVENOUS ADMINISTRATION

(Mr. D.S., No. 10)

. Whole Blood

⊙ Plasma

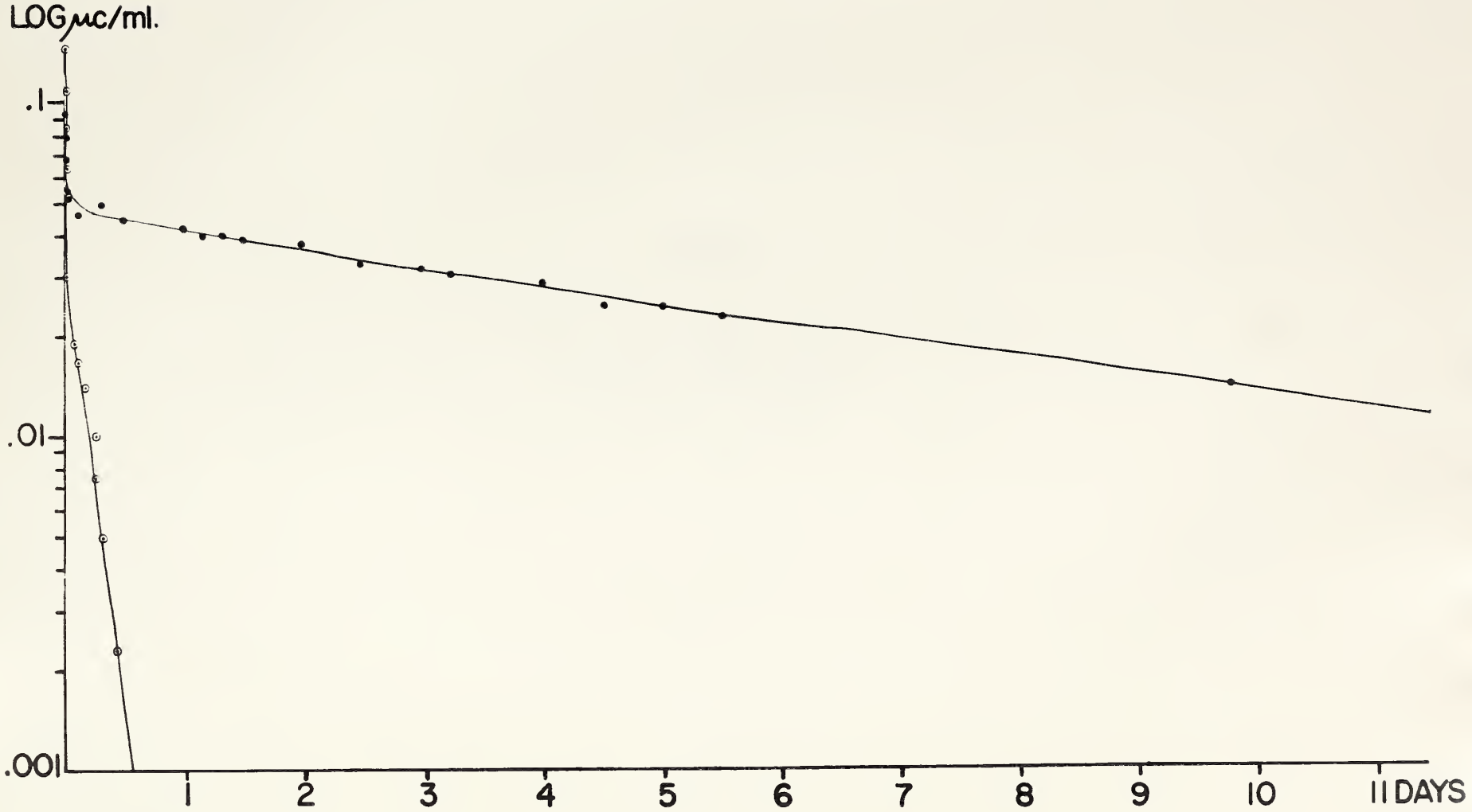

LOG μc/ml.
.1
.01
.001
1
2
3
4
5
6
7
8
9
10
11 DAYS

FIGURE 6

P^{32} CONTENT IN WHOLE BLOOD RELATED TO TIME

AFTER ORAL ADMINISTRATION

(Mr. W.T., No. 15)

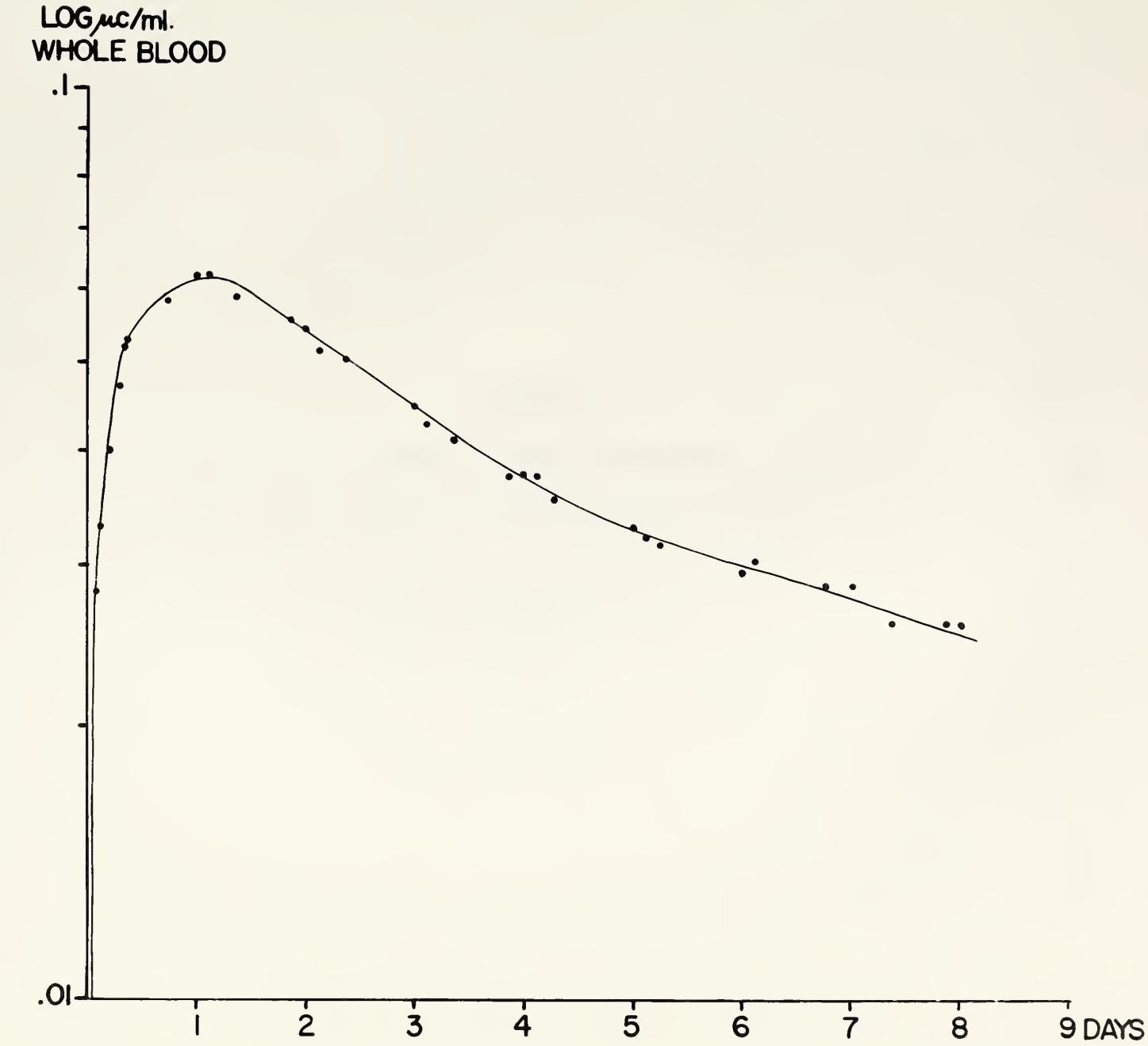

LOG μc/ml.
WHOLE BLOOD
.1
.01
1
2
3
4
5
6
7
8
9 DAYS

TABLE 9

RADIATION TO THE BLOOD AND OTHER HEMATOLOGICAL INFORMATION

FOR A SERIES OF 16 PATIENTS TREATED WITH P^{32}

* Non-polycythemic cases.

** Oral therapy.

Case No.	Patient	Sex	Length of Study (days)	Total Blood Volume (ml)	Red Cell Volume (ml)	Hematocrit before Therapy	Prior Phlebotomy within One Month (ml)	Dose (mc)	Total rad to Blood	rad/mc Administered
1	H.C.	F	21	5425	3255	69	No	6.07**	35.12	5.79
2	L.M.	M	6	5385	3231	53	1200	5.00	12.17	3.04
3	L.R.	M	27	7330	3885	55	1000	4.50	24.00	5.33
4	W.M.	M	15	5389	3126	58	2500	4.50	19.40	4.31
5	J.L.	M	5	5190	4204	81	No	4.50	38.97	8.66
6	T.M.	M	23	5780	3179	55	1000	4.52	28.72	6.35
7	W.C.	M	22	5550	3052	55	No	4.00	15.38	3.84
8	T.K.	F	11	5425	2875	54	1000	3.97	28.37	7.42
9	T.H.*	M	26	3540	1522	43	No	4.00	26.05	6.51
10	D.S.	M	24	5455	3055	53	2400	4.00	18.87	4.72
11	C.H.	F	19	3403	2076	56	1400	4.00	20.40	5.10
12	F.Mc.	F	25	5588	2914	62	1200	3.50	19.44	5.55
14	H.S.*	M	27	4274	1387	39	No	0.48**	0.92	1.93
15	W.T.	M	9	8050	5635	66	350	6.00**	17.38	2.90
16	T.J.	M	39	6900	4550	53	3000	4.50	26.74	5.94
17	B.T.	F	23	5722	3662	64	No	4.50	39.51	8.78

DISCUSSION

Urine

The average urinary excretion of P^{32} as a percentage of the initial dose to the end of 3 days for our complete series was 14.7% with limits of 6.4 and 18.7%. The corresponding 5 day average amounted to 18.0% with limits of 7.5% and 22.5%.

As previously pointed out, our series consisted of 12 polycythemic and two non-polycythemic patients. In the polycythemias the average for 3 day urinary excretion was 15.1%. The 5 day average was 18.6% with limits in both cases unchanged. In the non-polycythemias the average 3 day excretion was 12.4%. The 5 day figure was 14.6%. The difference between these two classes of cases cannot be shown to be significant in view of the small series. The range of the entire series (which included the small percentage of fecal excretion which will be discussed later) is depicted (in terms of remaining body content) in Figure 7.

It is interesting to note (Table 4) that the maximum excretion of P^{32} always occurs within the first 24 hrs. There is a positive correlation between the 5 day total and the first day percentage (e.g., an average value for the first 24 hrs. indicates an average retention of the therapy).

Although Hevesy, Erf and Lawrence are the only authors reporting excretion of both fecal and urinary P^{32} (their excretion values are shown in Figures 8 and 9, Appendix 2), one excellent

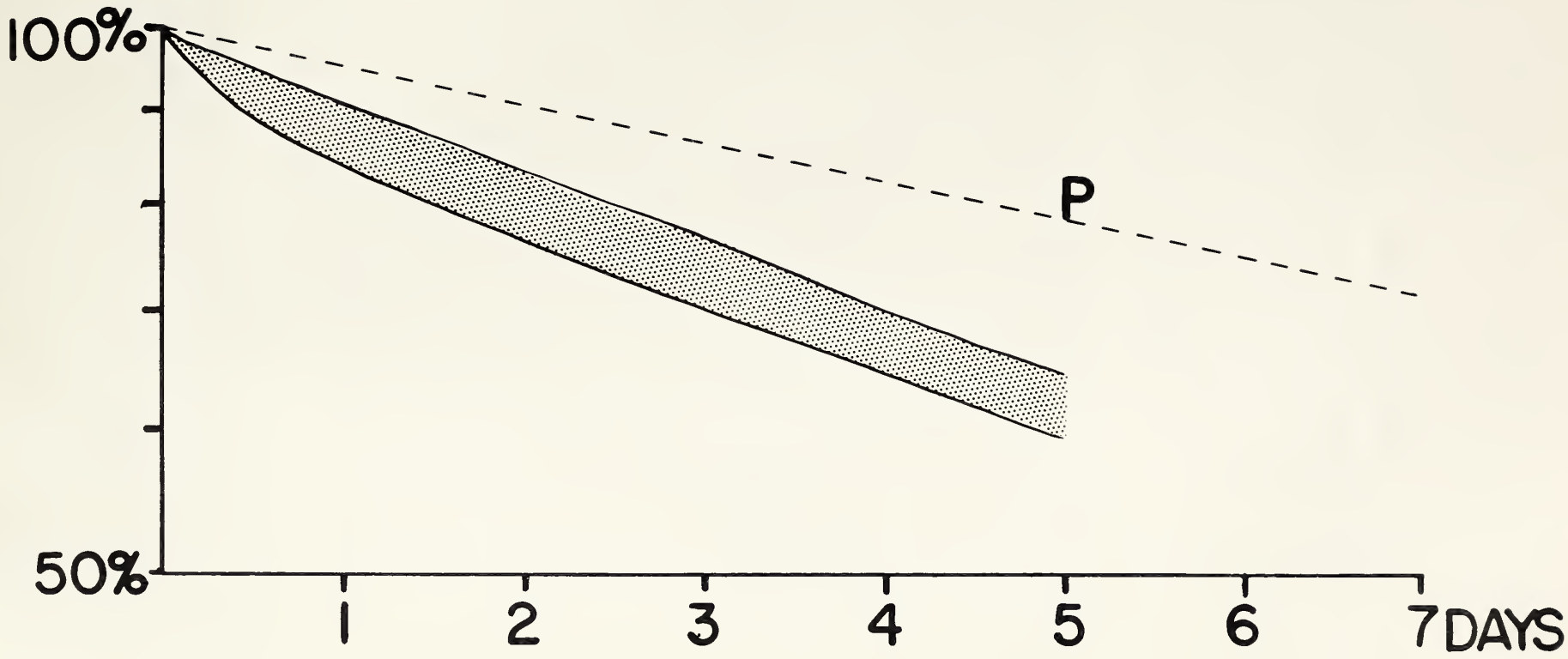
FIGURE 7

RANGE OF BODY CONTENT (DECAYED) WITH RESPECT TO TIME.

INITIAL THERAPY AS 100%.

(14 CASES, UNIVERSITY OF ALBERTA HOSPITAL)

----------^{P}---------- Natural Decay of P^{32}


100%
50%
P
1
2
3
4
5
6
7 DAYS

report of Szur, Lewis and Goolden, 1958 (28) gives a mean value and range for 48 hr. urinary excretion in 153 polycythemic cases treated intravenously with carrier free radiophosphorus. These results are reported in Table 10 (Appendix 2) and depicted diagrammatically in Figure 10. Bearing in mind that our series (Figure 7) is inclusive of a small amount of fecal excretion, our range for urinary excretion lies within the mean given by Szur et al.

The series of Erf and Lawrence (7) included three polycythemia (one treated intravenously and two orally), and four normals (two given phosphorous intravenously and two orally). However, the P^{32} was not carrier free, additional carrier in varying amounts was added and administration was under unspecified non-fasting conditions. Their 3 day average urinary excretion of P^{32} as a per cent of the initial dose in polycythemia cases was 5.32% (this is lower than our value, but well within the values noted by Szur et al.) and the corresponding figure for the four normals was 22.71%. This latter is higher than our figure (12.4%) but we feel that the results indicate that highest excretion in urine could be correlated with the highest relative addition of carrier despite the conclusion of Erf and Lawrence (7) that "patients with polycythemia excreted less than normal individuals in both urine and feces, regardless of the route of administration."

Hevesy (see Table 10) reported a series of 14 normal cases given intravenous P^{32} with added carrier and he obtained a mean value of 13% for the 24 hr. urinary excretion. Comparing Figure 8 with

Figure 10 and again with Figure 9, we see that the mean excretion is greater in the Hevesy series than in our or Szur's series but less than that of the normals of Erf and Lawrence. In other words, it would appear that a correlation may exist between the amount of urine excreted and the amount of the carrier added to the dose.

Stool

The average stool excretion in our series as a percentage of the initial dose to the end of 3 days was 1.4% with limits of 0.1 and 2.9%. The 5 day average was 2.4% with limits 0.5 and 4.9%. The 3 day average for the 11 intravenous cases was 1.5% and the average for the 3 oral cases was 1.3%. The oral administration in the latter cases was carried out under strict fasting conditions similar to those specified by Wiseman (33): viz., no food for 6 hours before or 3 hours after and a minimal amount of fluid.

Hevesy only reports two cases where the fecal excretion was followed, one of these was intravenous with a small amount of carrier and the 3 day value was 2.21% which is close to the result for our series. The other case was oral and the dose was mixed with the same amount of carrier but added to the patient's food. This gave a 3 day value of 12.6%.

Erf and Lawrence reported a 3 day average of 14.62% for 4 oral cases and a 3 day value of 0.55% for 3 intravenous cases. Our results (1.3%) are so much lower than those of Hevesy or Erf and Lawrence for oral administration that we investigated

the effect of allowing liquid intake before carrier free oral therapy and a normal meal one hour after therapy. In this case we found that the 3 day fecal excretion reached 25%. It is hard to say what effect additional carrier would have had on this figure, but in all probability it would have increased it. At any event, it is important to observe the fasting condition in order to cut down the fecal excretion.

Total Body Radiation

These values are directly proportional to the area under the total body content curve (Figure 4) and inversely proportional to the patient's mass. In our series of 14 cases (Table 5) the total body radiation over the first 6 days ranged from 6.9 - 16.3 rad. The radiation figures from time of initial dose to complete decay varied from a lower limit which lay between 21.32 and 25.44 rad and an upper limit of from 50.30 to 60.02 rad. These values lie below the level required to produce radiation sickness and no such instance was observed.

In terms of rad/mc. administered this gave a variation between a lower range of 5.33 - 6.36 rad/mc. and 8.24 - 9.89 rad/mc. from time of initial dose to complete decay.

Since the total body radiation is directly proportional to the area under the total body content curve, it is evident that the cases of Hevesy, and Erf and Lawrence would receive less total body radiation than did the cases in our series, but that the mean

value for the series of 153 cases of Szur et al. would be very close to that for our series. That is to say, for either carrier free intravenous therapy or for carrier free, fasting, oral therapy, the total body radiation to the patient will probably be very close to those figures for our series quoted above. Assuming that about the same amount of P^{32} is present in the gonadal tissue as in the average tissue at any time, then the genetic dose will lie in this same range, that is to say, in what is generally considered to be the range of the estimated doubling mutation rate in men (30 - 80 r).

Blood

The radiation to the blood was calculated for 16 cases and the individual values were found to lie between 1.93 rad/mc. and 8.78 rad/mc. (Table 9). This is quite a wide range of variation. No correlation was found to exist between total red cell volume and rad/mc. administered.

The total radiation to the blood in the polycythemic patients varied from 12.17 to 39.51 rad (Table 9). These figures are lower than those for total body radiation. No immediate suppression of the red cell count was noted in our series. The effect of the P^{32} is not seen for 60 - 100 days after therapy. Since the average life span of a red cell is from about 100 - 120 days it would appear that P^{32} halts cell division in the bone marrow and that the bone marrow is sensitive to relatively low radiation levels.

CONCLUSIONS

1. Under fasting conditions (both before and after the administration of the P^{32}) with little or no added carrier, the fecal excretion of P^{32} will be small. This will mean that the total excretion of P^{32} after oral administration will not differ significantly from the total excretion of P^{32} after intravenous administration of P^{32}.

   Under the fasting conditions of administration it should not be necessary to increase the oral dosage by 4/3 in order to attain the same clinical effect from the therapy.

2. Under uncontrolled conditions of oral administration, fecal excretion value can be expected to be as high or higher than those quoted by Erf and Lawrence.

3. To separate the carrier effect and before one can conclude that polycythemic patients have a higher phosphorus requirement than normal people, more normals should be studied.

4. The P^{32} content of the urine in the first 24 hrs. after therapy is a good indication as to whether or not a particular patient will retain the dose within normal limits.

5. Total body radiation values calculated according to the assumptions set out in this paper are not large enough to bring about radiation sickness in the average patient. If the genetic dose is considered as equal to the total body radiation, the figures lie in the mutation doubling range for man (30 - 80 r).

6. Radiation to the blood from therapeutic doses of P^{32} is small. The effect of P^{32} must in some way be due to the suppression of the mitotic activity of the precursor red cells in the bone marrow.

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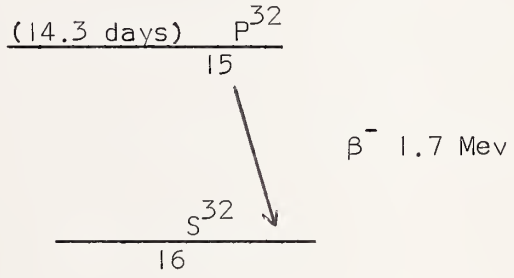
APPENDIX I

APPENDIX I

Radioactive phosphorus is prepared from the irradiation of pure sulphur with thermal neutrons in a nuclear reactor. P^{32} is formed from S^{32} with the absorption of a neutron and with the emission of a proton. P^{32} disintegrates back to S^{32} with the emission of a beta particle having a peak energy of 1.7 Mev. No gamma rays are emitted. The maximum penetration of beta particles in tissue is about 8 mm., the average penetration is about 2 mm. The half life of P^{32} is 14.3 days.

Disintegration scheme of radioactive phosphorous



APPENDIX 2

FIGURE 8

RANGE OF BODY CONTENT (DECAYED) WITH RESPECT TO TIME.

INITIAL DOSE AS 100% (15 CASES, HEVESY)

----------P---------- Natural Decay of P^{32}

Numbers 1-3, inclusive, refer to patients listed in Table 10

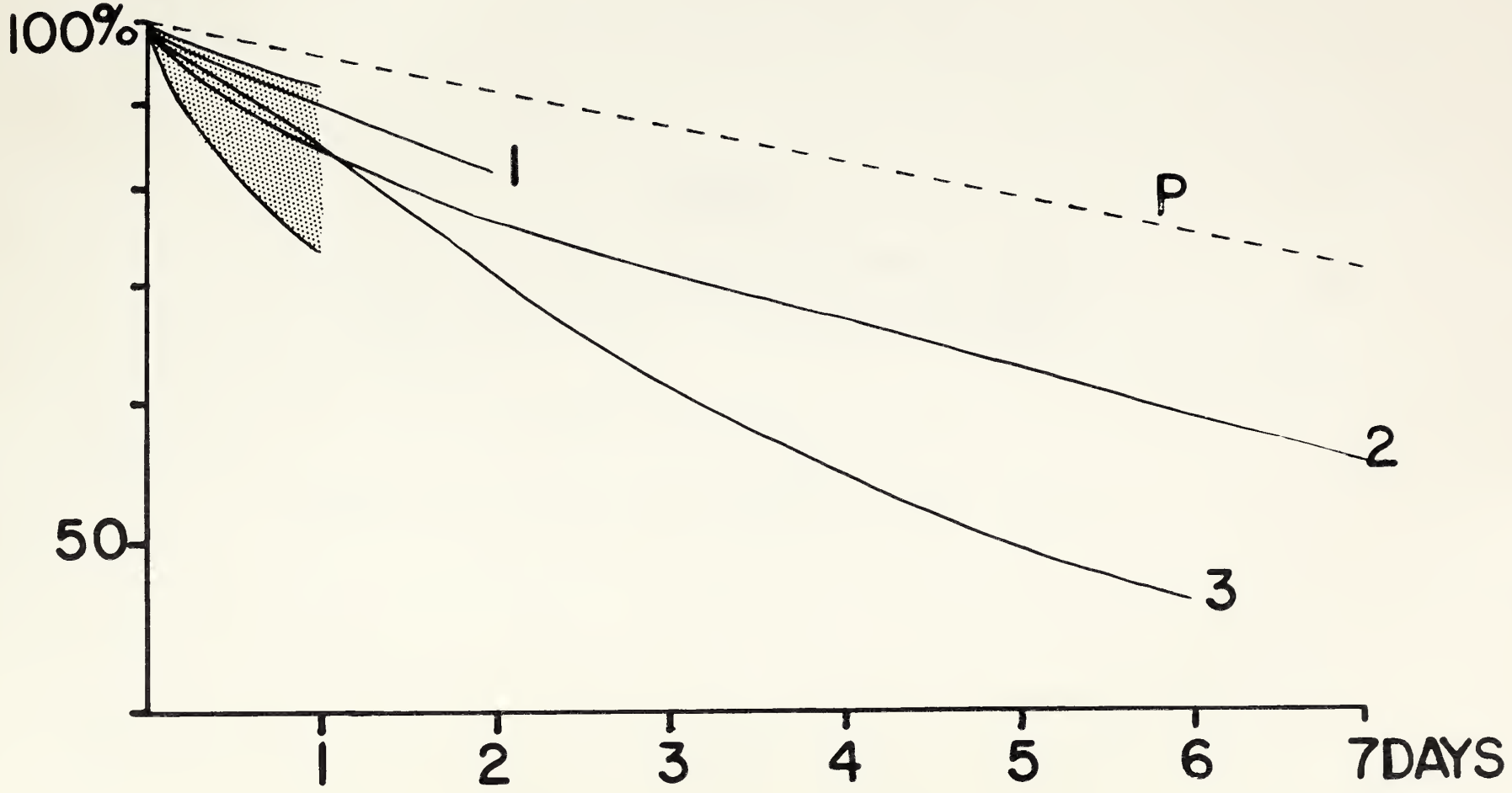

100%
50
1
P
2
3
1
2
3
4
5
6
7DAYS

FIGURE 9

RANGE OF BODY CONTENT (DECAYED) WITH RESPECT TO TIME.

INITIAL THERAPY AS 100%. (7 CASES, ERF AND LAWRENCE)

---P--- Natural Decay of P^{32}

Numbers 1-7, inclusive, refer to patients listed in Table 10

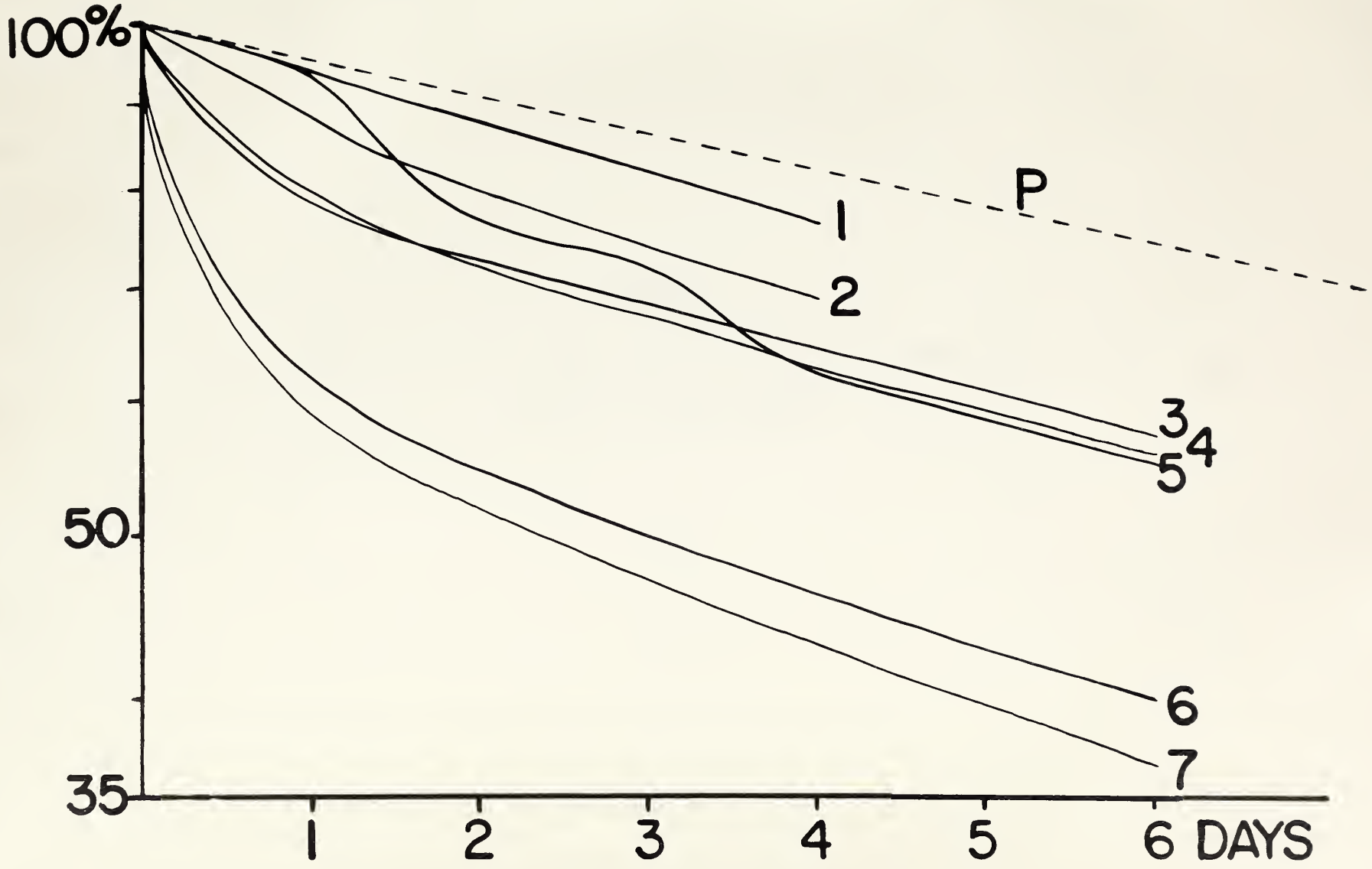

100%
50
35
P
1
2
3
4
5
6
7
1
2
3
4
5
6 DAYS

TABLE 10

EXCRETION OF P^{32} IN NORMAL CASES AND POLYCYTHEMIA RUBRA VERA

REPORTED BY OTHER AUTHORS

Case No.	Patient	Diagnosis	μc Dose	mg Carrier	Days Studied		Daily Excretion as % of Initial Dose								Total to end of 3 days	Total to end of 5 days
Erf and Lawrence (7)						Day	1	2	3	4	5	6	7	8		
1	Wer. 9	Polycythemia rubra vera intravenous	2550	167	4	Urine	1.0	2.31	1.44	.91					4.75	-
						Stool	.04	.21	.28	.27					.53	-
						Total	1.04	2.52	1.72	1.18					5.28	
2	Wer. 9	Polycythemia rubra vera oral	2550	178	4		6.97	2.23	.91	1.70					10.11	-
							.24	3.16	.55	.15					3.95	-
							7.21	5.39	1.46	1.85					14.06	
3	Mie. 1	Normal Oral	1500	600	6		4.63	1.7	.89	.72	.74	.45			7.22	8.68
							12.93	.52	.22	.02	-	.06			13.67	13.69
							17.56	2.22	1.11	.74	.74	.51			20.89	22.37
4	Hay. 5	Polycythemia rubra vera oral	5960	2800	6		.6	.3	.2	.2	.1	.1			1.10	1.40
							15.3	-	7.5	-	-	-			15.3	22.8
							15.9	.3	7.7	.2	.1	.1			16.40	24.20
5	Vic. 4	Normal intravenous	1500	600	6		16.66	3.5	1.5	1.48	1.27	1.06			21.66	24.41
							.08	.45	-	-	.02	.01			.53	.55
							16.74	3.95	1.5	1.48	1.29	1.07			22.19	24.96
6	Rob. 1	Normal oral	1500	600	6		12.7	1.96	2.12	1.15	1.41	1.12			16.78	19.34
							22.59	2.59	.39	.10	.01	.01			25.57	25.68
							35.29	4.55	2.51	1.25	1.42	1.13			42.35	45.02
7	Per. 2	Normal intravenous	1500	600	6		37.66	5.03	2.48	1.69	1.74	1.16			45.17	48.60
							.098	.25	.24	.16	.02	.05			.59	.77
							37.76	5.28	2.72	1.85	1.76	1.21			45.76	49.37

Table 10 (continued)

Case No.	Diagnosis	μc Dose	mg Carrier	Days Studied		Daily Excretion as % of Initial Dose										Total to end of 3 days	Total to end of 5 days
Hevesy (4, 10)					Day	1	2	3	4	5	6	7	8	9	10		
1	(1939) Normal	fasting	-	2	Urine	6.8	3.3										
					Stool	no record											
					Total	6.8	3.3										
2	(1937) Normal intravenous	.5 mg P^{32}	-	10		12.5	3.1	2.9	-	1.6	-	2.2	-	0.6	1.8	18.50	20.1
						.24	1.6	.37	.3	-	-	-	-	-	-	2.21	2.5
						12.74	4.7	3.27	.3	1.6	-	2.2	-	0.6	1.8	20.71	22.6
3	(1937) Normal oral	.5 mgm labelled P^{32} in food	-	6		11.0	2.8	2.8	2.4	2.7	1.8					16.6	21.7
						-	7.0	5.6	1.8	1.1	-					12.6	15.5
						11.0	9.8	8.4	4.2	3.8	1.8					29.2	37.2
12 cases	(1939) Normal intravenous	100 μc	1 mg	1		Mean value 13% Range 4.0% to 23.0% No stool											
Szur, Lewis and Goolden (28)																	
153 cases	Polycythemia rubra vera intravenous	3500 to 7000	None	2	Urine	Mean value 10.4 ± 4.3% Range, 3% to 30.7%											
					Stool	No record											

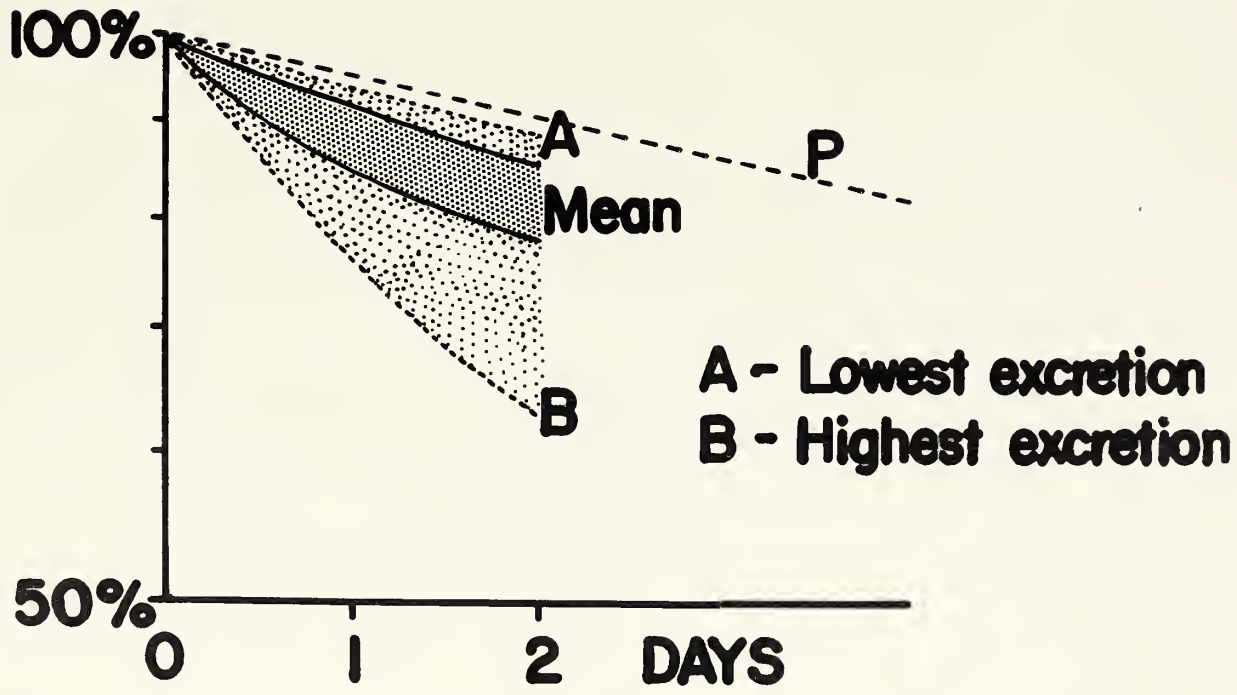
FIGURE 10

RANGE OF BODY CONTENT (DECAYED) WITH RESPECT TO TIME.

INITIAL DOSE AS 100%.

(153 CASES, URINE ONLY, SZUR, LEWIS AND GOOLDEN)

---------- Natural Decay of P^{32}


100%
50%
A
P
Mean
B
A - Lowest excretion
B - Highest excretion
0
1
2
DAYS